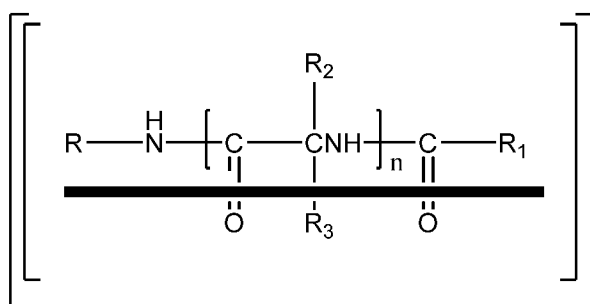


## IN THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the present application.

1. (currently amended) A method for preventing or treating a condition associated with cortical spreading depression (CSD) in a subject, comprising administering to the subject, in an amount effective to suppress CSD, a compound having the **Formula**

**(Ib)**



**Formula (Ib)**

wherein

~~R is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, aryl, aryl lower alkyl, heterocyclic, heterocyclic lower alkyl, lower alkyl heterocyclic, lower cycloalkyl or lower cycloalkyl lower alkyl, and R is unsubstituted or is substituted with at least one electron withdrawing group or at least one electron donating group;~~

~~R<sub>1</sub> is hydrogen or lower alkyl, lower alkenyl, lower alkynyl, aryl lower alkyl, aryl, heterocyclic lower alkyl, lower alkyl heterocyclic, heterocyclic, lower cycloalkyl, lower cycloalkyl lower alkyl, each unsubstituted or substituted with at least one electron donating group or at least one electron withdrawing group;~~

~~R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, aryl lower alkyl, aryl, halo, heterocyclic, heterocyclic lower alkyl, lower alkyl heterocyclic, lower cycloalkyl, lower cycloalkyl lower alkyl, or Z-Y, wherein R<sub>2</sub> and~~

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~~R<sub>3</sub> may be unsubstituted or substituted with at least one electron withdrawing group or at least one electron donating group; and wherein heterocyclic in R<sub>2</sub> and R<sub>3</sub> is furyl, thienyl, pyrazolyl, pyrrolyl, methylpyrrolyl, imidazolyl, indolyl, thiazolyl, oxazolyl, isothiazolyl, isoxazolyl, piperidyl, pyrrolinyl, piperazinyl, quinolyl, triazolyl, tetrazolyl, isoquinolyl, benzofuryl, benzothienyl, morpholinyl, benzoxazolyl, tetrahydrofuryl, pyranlyl, indazolyl, purinyl, indolinyl, pyrazolindinyl, imidazoliny, imidazolindinyl, pyrrolidinyl, furazanyl, N-methylindolyl, methylfuryl, pyridazinyl, pyrimidinyl, pyrazinyl, pyridyl, epoxy, aziridino, oxetanyl, azetidiny or, when N is present in the heterocyclic, an N-oxide thereof;~~

~~Z is O, S, S(O)<sub>a</sub>, NR<sub>4</sub>, NR<sub>6</sub>', PR<sub>4</sub> or a chemical bond;~~

~~Y is hydrogen, lower alkyl, aryl, aryl lower alkyl, lower alkenyl, lower alkynyl, halo, heterocyclic, heterocyclic lower alkyl, lower alkyl heterocyclic and Y may be unsubstituted or substituted with at least one electron donating group or at least one electron withdrawing group, wherein hetrocyclic has the same meaning as in R<sub>2</sub> and R<sub>3</sub> and, provided that when Y is halo, Z is a chemical bond, or~~

~~Z-Y taken together is NR<sub>4</sub>NR<sub>5</sub>R<sub>7</sub>, NR<sub>4</sub>OR<sub>5</sub>, ONR<sub>4</sub>R<sub>7</sub>, OPR<sub>4</sub>R<sub>5</sub>, PR<sub>4</sub>OR<sub>5</sub>, SNR<sub>4</sub>R<sub>7</sub>, NR<sub>4</sub>SR<sub>7</sub>, SPR<sub>4</sub>R<sub>5</sub>, PR<sub>4</sub>SR<sub>7</sub>, NR<sub>4</sub>PR<sub>5</sub>R<sub>6</sub>, PR<sub>4</sub>NR<sub>5</sub>R<sub>7</sub>, N<sup>+</sup>R<sub>5</sub>R<sub>6</sub>R<sub>7</sub>, NR<sub>4</sub>C-R<sub>5</sub>, SCR<sub>5</sub>, NR<sub>4</sub>C-OR<sub>5</sub>, SC-OR<sub>5</sub>;~~

$$\begin{array}{cccc} \text{---} & \text{---} & \text{---} & \text{---} \\ & \parallel & \parallel & \parallel \\ & \text{O} & \text{O} & \text{O} \end{array}$$

~~or NR<sub>4</sub>NR<sub>5</sub>-C-OR<sub>6</sub> ;~~

$$\begin{array}{c} \text{---} \\ \parallel \\ \text{O} \end{array}$$

~~R<sub>6</sub>' is hydrogen, lower alkyl, lower alkenyl, or lower alkynyl which may be unsubstituted or substituted with at least one electron withdrawing group or at least one electron donating group;~~

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~~R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> are independently hydrogen, lower alkyl, aryl, aryl lower alkyl, lower alkenyl, or lower alkynyl, wherein R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> may independently be unsubstituted or substituted with at least one electron withdrawing group or at least one electron donating group;~~

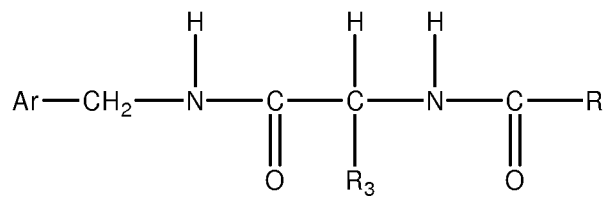
~~R<sub>7</sub> is R<sub>6</sub> or COOR<sub>8</sub> or COR<sub>8</sub>, which R<sub>7</sub> may be unsubstituted or substituted with at least one electron withdrawing group or at least one electron donating group;~~

~~R<sub>8</sub> is hydrogen or lower alkyl, or aryl lower alkyl, and the aryl or alkyl group may be unsubstituted or substituted with at least one electron withdrawing group or at least one electron donating group;~~

~~n is 1-4; and~~

~~a is 1-3,~~

Formula (IIb)



Formula (IIb)

wherein

Ar is phenyl which is unsubstituted or substituted with at least one halo group;

R<sub>3</sub> is CH<sub>2</sub>-Q, wherein Q is lower alkoxy containing 1-3 carbon atoms;  
and

R<sub>1</sub> is lower alkyl containing 1-3 carbon atoms,

or a pharmaceutically acceptable salt thereof.

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2. (currently amended) The method of claim 1, wherein the CSD-associated condition is a chronic headache.
3. (currently amended) The method of claim 1, wherein the CSD-associated condition is a migraine.
4. (currently amended). The method of claim 3, wherein the migraine is an acute migraine.
- 5-13. (cancelled)
14. (currently amended) The method of claim 1, wherein the compound is  
(R)-2-acetamido-N-benzyl-3-methoxypropionamide;  
O-methyl-N-acetyl-D-serine-m-fluorobenzylamide; or  
O-methyl-N-acetyl-D-serine-p-fluorobenzylamide[[]];  
~~N-acetyl-D-phenylglycinebenzylamide;~~  
~~D-1,2-(N,O-dimethylhydroxylamino)-2-acetamido——acetic——acid~~  
~~benzylamide; or~~  
~~D-1,2-(O-methylhydroxylamino)-2-acetamido-acetic-acid-benzylamide.~~
15. (cancelled).
16. (currently amended). The method of claim ~~[[15]]~~ 1 wherein, in the compound of Formula (IIb), Ar is unsubstituted phenyl.
17. (currently amended) The method of claim ~~[[15]]~~ 1 wherein, in the compound of Formula (IIb), halo is fluoro.
18. (currently amended) The method of claim ~~[[15]]~~ 1 wherein, in the compound of Formula (IIb), R<sub>3</sub> is CH<sub>2</sub>-Q, wherein Q is alkoxy containing 1–3 carbon atoms and Ar is unsubstituted phenyl.
19. (cancelled)
20. (currently amended). The method of claim ~~[[19]]~~ 1, wherein the compound is substantially enantiopure.
- 21-23. (cancelled).
24. (currently amended) The method of claim 1, wherein the compound of Formula (IIb) is (R)-2-acetamido-N-benzyl-3-methoxypropionamide or a

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pharmaceutically acceptable salt thereof

25. (previously presented) The method of claim 24, wherein the compound is substantially enantiopure.
26. (previously presented) The method of claim 1, wherein the compound is administered at a dose of at least 100 mg/day.
27. (previously presented) The method of claim 1, wherein the compound is administered at a dose of at a maximum 6 g/day.
28. (previously presented) The method of claim 1, wherein the compound is administered at increasing daily doses until a predetermined daily dose is reached which is maintained during further treatment.
29. (previously presented) The method of claim 1, wherein the compound is administered in at most three doses per day.
30. (currently amended) The method of claim 1, wherein administration of the compound results in a plasma concentration of 7 to 8 µg/ml (trough) and 9 to 12 µg/ml (peak), ~~calculated as an average over a plurality of treated subjects.~~
31. (previously presented) The method of claim 1, wherein the compound is administered for at least one week.
32. (previously presented) The method of claim 1, wherein the compound is administered orally.
33. (currently amended) The method of claim 1, further comprising administering to the subject a further active agent effective for prevention or treatment of a headache or a CSD-associated disorder~~[[s]]~~.
34. (currently amended) The method of claim 33, wherein the compound of Formula (Ib) and the further active agent are present in a single dose form.
35. (previously presented) The method of claim 1, wherein the subject is a mammal.
36. (previously presented) The method of claim 35, wherein the subject is human.
37. (currently amended) A therapeutic combination comprising
  - (a) a compound of Formula (Ib), and

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(b) a further active agent effective for prevention or treatment of ~~of~~  
~~treatment~~ of a headache or a CSD-associated disorder~~[[s]]~~.

38. (currently amended) The combination of claim 37, wherein the compound of Formula (Ib) and the further active agent are present in a single dose form.

39. (currently amended) The combination of claim 37, wherein the compound of Formula (Ib) and the further active agent are present in separate dose forms.

40. (currently amended) The method of claim 33, wherein the compound of Formula (Ib) and the further active agent are present in separate dose forms.

41. (new) The method of claim 2, wherein the chronic headache is selected from a group consisting of a muscle contraction headache, a toxic headache, a cluster headache, a traction headache, or an inflammatory headache.

42. (new) The method of claim 1, wherein the compound is administered at a dose of at a maximum 1 g/day.

43. (new) The method of claim 1, wherein the compound is administered at a dose of at a maximum 400 mg/day.

44. (new) A method of suppressing CSD thereby preventing a migraine in a subject, the method comprising orally administering to the subject (R)-2-acetamido-N-benzyl-3-methoxypropionamide.

45. (new) The method of claim 44, wherein (R)-2-acetamido-N-benzyl-3-methoxypropionamide is orally administered at a dose of at least about 100 mg/day to a maximum of about 1 g/day.

46. (new) A method of preventing or treating a headache selected from the group consisting of a muscle contraction headache, a toxic headache, a cluster headache, a traction headache, or an inflammatory headache, the method comprising administering to the subject an oral effective amount of (R)-2-acetamido-N-benzyl-3-methoxypropionamide.

47. (new) The method of claim 46, wherein the headache is cluster headache.

48. (new) The method of any one of Claims 44 to 47, further comprising administering to the subject a triptan.

49. (new) The method of claim 48, wherein the triptan is sumatriptan.

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50. (new) The combination of claim 37, wherein the compound of Formula IIb is (R)-2-acetamido-N-benzyl-3-methoxypropionamide.
51. (new) The combination of claim 37, wherein the further active agent effective for prevention or treatment of a headache or a CSD-associated disorder is a triptan.
52. (new) A method of suppressing CSD in a subject, the method comprising orally administering to the subject about 100 mg/day to about 400 mg/day (R)-2-acetamido-N-benzyl-3-methoxypropionamide.